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SYPHILIS

AND ITS

TREATMENT



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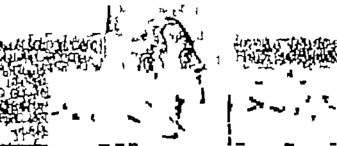
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I

Course of the disease.

SYPHILIS is a chronic infectious disease which is acquired usually through sexual intercourse—hence the name "Venereal"

The first reliable record of its occurrence in Europe dates as far back as the end of the 15th century but up to the beginning of the 20th century i.e., during more than 400 years, no treatment for this malady was known to the world, except by mercury It was only through the discovery of the causal agent of syphilis by Schaudinn and Hoffmann (1905) and the production of Salvarsan by Professor Ehrlich that the treatment of syphilis received new impetus. A new therapeutic era was thus opened up.

Causal Agent.

The disease is caused by a macroscopic animal called *spirochaeta pallida* (*Plate Nos* 3 *and* 4) belonging to the protozoa group As seen in the living condition, under the microscope, the spirochaeta is a long thread-like organism tapering at

both ends, with 8—16 cork-screw like spirals which give it a twisted appearance. The organism is found in all lesions but most abundantly in the situation where the infectivity is most intense, for instance, mucous nodules and condylomata.

Mode of Infection.

Infection takes place by direct contact only

An abrasion, however slight, on the surface is necessary for the introduction of the spirochaeta into the system. Even the mucous membrane, if intact, resists infection. Apart from sexual intercourse, infection in some rare cases may also be acquired in other ways, for instance, through the hands of doctors and midwives, kisses, etc. Further syphilis can be transmitted from mother to the child through an infected placenta or milk. The *incubation period*, i.e., the time between the getting of the infection and the first appearance of symptoms, is about three weeks.

Clinical Symptoms.

The course of syphilis is characterised by three well marked stages and has a distinct clinical significance.

Primary Lesions (First Stage).

The main characteristic of this stage is that the disease remains localized at the site of the infection and in the regional lymph nodules

The first sign of the disease is a hard, painless papule with an indurated base at the site of the

Plate No. 1



E. HOFFMANN

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The first sign of the disease is a hard papule with an indurated base at the site of the

infection—the so-called primary sore (*Plate No. 5*) In man it is generally single and in woman it is often multiple. The chancre or "hard sore" as it is called, is the expression of the local reaction of the tissues to the invasion of the spirochaets. The chancre looks like a superficial knot to start with, but very soon grows in size. It is generally of a reddish-brown or grey colour and feels like hard parchment. Inasmuch as it is painless and gives only a slight discharge it may pass unobserved by the patient. Sometimes it undergoes central ulceration, the surface of which shows a fatty shining yellow colour the reddish-brown walls at the peripheri are very hard, and when pressed between the fingers, reveal a hard infiltration at the base.

In 99 out of 100 cases the genitals are the favourite site of the primary sore—in male, the groove behind the glans, and the frenulum of the prepuce in female, the vulva or the clitoris. In rare cases, lips, tongue, tonsils, and under very exceptional circumstances, anus, breast or finger may also become the site of the sore. In certain cases of primary ulcer complications such as oedema or swelling of the loose skin of the penis or that of the vulva may occur This swelling also feels hard and is painless. Another characteristic sign of this stage is the painless swelling of the dorsal lymphatic vessel of the penis. Regional lymph glands may also be swollen but not painful. The primary ulcer *with or without any specific treatment*, disappears leaving behind a pigmented, rather hard, scar

Generalized swelling of the lymphatic glands, *e.g.*, cubital, axillary and paramaxillary is usually seen in five weeks after the primary sore, *i.e.*, about nine weeks after the infection and marks the beginning of the second stage.

Secondary Lesions (Second Stage).

During this stage various kinds of eruptions appear almost exclusively on the skin, showing thereby that the disease has become generalized in the system.

This is due to the fact that the parasites are carried away from the site of the infection to the various parts of the body by the lymphatics and subsequently by the blood stream. The onset of this stage is characterised by slight fever headache, pain in joints and muscles. Generally speaking, the subjective well being of the patient is not significantly disturbed although severe prostration may be sometimes met with.

This stage extends over 2—3 years and is divisible into two —

Early and late, according to the early or late appearance of the symptoms and to the site of appearance.

Early Local Symptoms. Macular exanthema (roseola) or papulary eruptions appear on the skin. The term roseola is applied to small oval or round patches of dirty reddish-brown colour These do not project beyond the skin surface through the pressure of a glass spoon these may be

made to disappear Roseola is generally situated on the extensor sides of the arms, trunk of the body and lateral sides of the chest, and the abdomen.

The papules, on the other hand, appear in small or big hard knots on the skin, having a round shape. At the time of appearance they are reddish-brown but later on they become distinctly brown.

All these eruptions, roseola or papules disappear after some time, the former earlier than the compact papules, leaving behind, especially in females, white irregular patches with ill-defined margins, which extend from the neck to the body These patches persist for years, and are known as syphilitic leucoderma (true leucoderma is distinguished by having well-defined margins).

Late Local Symptoms. In the late secondary stage the subjective well-being of the patient is only rarely disturbed. The eruptions, which are characterised by their polymorphic nature (*Plate No* 6), come and go but *never on the same spot more than once* in other words, every eruption confers a local skin immunity to the site of its occurrence. In this way the entire skin may get a blotchy appearance.

Of the different forms of eruptions during this stage, the papular forms are of a weeping type, oozing out a dirty secretion. These eruptions are very superficial with broad surfaces and tend to be confluent thereby forming plaques. These papules usually develop on the genitals, arms and the surrounding regions (condylomata). *Plate No* 7

They are very irritating on account of the unavoidable friction encountered. The surface of these papules looks greyish owing to the secretion which oozes out and which contains numerous spirochaetes. Sometimes these papules develop into small abscesses.

In some cases, the papular eruptions may develop into what are known as pustules. These affect the deeper layers of the skin. The pustular type of eruption resembles impetigo and is characterised by purulent exudation.

The palms and the soles, as well as the skin of the head, may also be affected. The exudative forms such as papules or pustules are frequently accompanied by more or less, intense itching

Another rather frequent type of skin eruption encountered in the late secondary stage, is the small papular form appearing in groups at the back and medial surface of the thigh and resembling typical lichen" and hence known as syphilitic lichen. They are generally a little moist and give rise to crusts.

Tertiary Lesions (Third Stage).

The third stage is characterised by the fact that the generalized infection of the second stage once again becomes localized in well-defined tissues

The reason for this is that towards the end of the secondary stage, or at the beginning of the third stage the skin has acquired a tissue immunity and, therefore does not show any more generalized eruptions. If at all the eruptions are solitary and of a destructive character extending into the

deeper layers of the skin. Besides the skin the internal organs such as bones, liver kidneys, heart blood vessels, central nervous system, etc., are also affected, resulting in the appearance of a particular form of granulation tissue. This granulation tissue may occur in two forms —

(1) a diffuse infiltration called "syphiloma,"

(2) a concentrated infiltration called "gumma."

Syphiloma. This is the general name for the skin eruptions in the tertiary stage. These are comparatively superficial and consist of massive infiltrations along the whole depth of the skin and have the characteristic syphilitic colour The infiltrations spread in various directions in the skin, *forming* ulcers. These ulcers while *progressive* at one end heal at the other Festoon-like scars are thus formed at the site.

Gumma (*Plate No* 8) As has been noted above, gumma is a concentration of peculiar granulation tissue with sharp and uneven edges and may develop in any organ. If situated on the exposed surface, that is, if of cutaneous or subcutaneous origin, it always affects the deeper layers of the tissues resulting in a hard infiltrate of the size of an egg. The infiltrates finally undergo necrosis (from syphilitic endarteritis and subsequent thrombosis of the supplying arteries) and form ulcers of livid colour Secretion from these ulcers is not purulent but rather resembles mucus. Such ulcers may spontaneously heal up however with deformities, or they may penetrate further and affect the muscles and the bones.

Of the tertiary affections of the inner organs coming within the sphere of the physician or the surgeon the most important ones are —

(1) *Weeping Papules.*—Weeping papules situated on the mucous membrane of the mouth and the nose, which appear first in the late secondary stage, affect the deeper tissues causing ulceration. In the tertiary stage they tend to destroy the neighbouring bones as well (perforation of the nasal septum and the hard palate, gumma of the pharyngeal wall)

(2) *Bones.*—The bones of the skull, tibia and the phalanges are most affected. In the long bones the infection gives rise to periostitis which brings about a softening of the bone tissue resulting sometimes in a spontaneous fracture.

Joints.—All forms of joint affections may result, such as pain, effusions and functional disturbances. Even structural derangement with intolerable pain is observed, the most affected areas being the knees and the smaller joints.

(3) *Circulatory System.*—Syphilitic affections of the arteries are most commonly met with. If the coronary arteries are affected the well-known angina pectoris develops. In the aorta and other big trunks it may lead to aneurysm while if peripheral arteries are affected, closure of the arterial lumen (endarteritis obliterans) with all the sequelae of blood stasis, necrosis etc. occurs.

(4) *Eyes.*—Iritis and Optic neuritis, atrophy of the optic nerve may occur

(5) *Ears.*—Apart from the external ear the eustachian tube is liable to be involved. In most

of the cases the acoustic nerve and the vestibular system are affected.

(6) *Reproductive organs*.—Of the different parts the testicles are most commonly involved giving rise to orchitis. One or both the testicles may be affected. The affection manifests itself in swollen and indurated testicle rather hard and painless although a tender spot is present on the anterior surface (as distinguished from epididymitis with pain on the posterior surface).

Diffuse interstitial infiltration of the vascular and connective tissues of the tubules brings about secondary sclerosis and therewith destruction of the spermatogenic tissues. Impotence and sterility are thus the end result.

(7) *The Nervous System*.—The nervous system may be involved at any time between 2—25 years after the infection. It frequently occurs within the first two years after the infection and the frequency of its occurrence diminishes with each successive year.

All the syphilitic diseases of the central nervous system are due to the direct action of the *S. pallidum*. They fall in two sharply separate classes, the interstitial and the parenchymatous. In the former the spirochaetes infect interstitial structures such as walls of the arteries and the meninges producing endarteritis and chronic meningitis respectively. General syphilitic inflammation of the brain, syphilitic meningitis, myelitis belong to this group.

T the second group belong diseases such as tabes dorsalis, general paralysis of the insane and syphilitic primary optic atrophy. In these cases, the parasite takes up its abode between the individual nerve cells, causing primary parenchymatous degeneration.

Congenital Syphilis. (Plate No. 9)

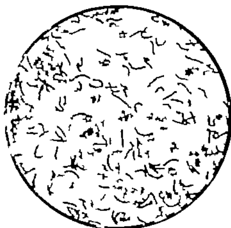
It has been observed before that the child can get the infection from the mother through an infected placenta or through milk. 2/5 of the cases of still-birth are to be attributed to hereditary syphilis. In case a syphilitic child is born alive it is usually very ill and a certain percentage of these dies shortly after the confinement. The main symptom is the swelling of the lymph glands, the liver and the spleen.

Such children who remain alive usually show the typical symptoms of the secondary stage as the primary one is completed before birth. The skin shows polymorphic eruptions in some of these cases the eruptions affect the face also which however is not usual in the second stage of the acquired syphilis.

The genital area the buttocks, the palms and the soles may also be found severely affected. It is not very unusual to find the destructive process of the disease already developed to an extent showing most of the characteristic pathological changes of the third stage for instance, general alopecia, malformation of the bones (depressed bridge of nose), nails and (Hutchinson's) teeth and the involvement of the mucous membrane. The eyes and the ears may also be affected.

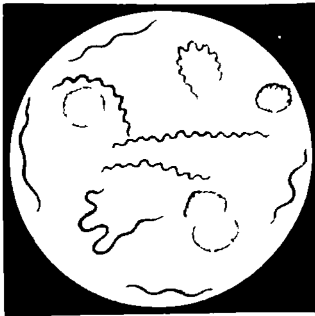
In the foregoing the most important clues for clinical diagnosis of the various stages are given. As regards specialised laboratory methods, including microscopical examination of the discharge for the confirmation of the presence of spirochaetes, or for the various serological methods such as Wassermann or Kahn test, for which suitable antigens are *supplied by "Behring Institute,"* the reader may refer to the text-books on this subject.

Plate V 1



Spirochaete Pallida (Low Power).

Plate No. 4



Spirochaeta Pallida (High Power)

II

Treatment of Syphilis.

SYPHILIS, as has been already explained, is one of the most dangerous and destructive infectious diseases; and since doctors are the keepers of national health, it is their duty to warn the syphilitic patient who is generally unaware of his being a source of danger to his family and thereby to the rest of the community. All necessary steps to be observed during the course of treatment and other precautions regarding diet, etc., should be clearly and convincingly explained. The patient should be warned from mixing with other people and must have a separate set of utensils meant exclusively for his own use. Apart from medical treatment, all the general hygienic precautions are strictly to be observed so as to assist the systematic treatment in attaining a speedy cure and thus saving all his fellowmen from the perils of this horribly dirty disease.

General Precaution.

It is advisable to treat such patients under control in a hospital, if possible. As the disappearance of symptoms does not give any definite clue as to the effects of the treatment, the state of the disease should be tested now and then through Wasser mann or Kahn reaction. During the course of an anti-syphilitic treatment the patient must live a very regular and temperate life. He must pay sufficient attention to the cleanliness of his mouth, throat, teeth and skin. Smoking and drinking

should be given up, or at least be sufficiently limited. He must be given a nourishing food. Physical and mental exertions are to be avoided during the course of the treatment although regular exercise is very important.

Systematic Treatment.

With the discovery of Salvarsan ('606') by Ehrlich in 1909 the era of specific treatment of syphilis was ushered in. Nowadays, systematic treatment consists absolutely in the applications of Salvarsan preparations and bismuth the latter in some cases, is replaced by mercury Excellent as the results with the first chemotherapeutic ('606') are, the handling of Salvarsan is too complicated for the general practitioners it requires certain preparatory manipulations which, if not properly done, always lead to unpleasant by-effects.

Only after Ehrlich succeeded in preparing what is nowadays known as Neosalvarsan ('914') that the specific treatment became the common property of the profession. Neosalvarsan being neutral in reaction, can be handled without any great preliminary operations as are required in case of Salvarsan'

For the general practitioners, two preparations mainly come into consideration, namely—

(1) Neosalvarsan
(2) Solu-Salvarsan
(both manufactured in Hoechst).

In the following we give a short account of these preparations

Neosalvarsan

It is an organic arsenic compound with a well defined chemical formula. It is available as a canary yellow powder in hermetically sealed ampoules. It dissolves quite easily in water and contains about 18.5—19.5 per cent. arsenic, *the maximum amount consistent with safety*. Neosalvarsan is injected *intravenously* only.

Solutions of Neosalvarsan should always be made with re-distilled sterile water. Solutions must be made freshly every time and should *on no account be left standing* since the solution easily oxidises when exposed to air. (*Plate No.* 10.)

Oxidised Neosalvarsan

The oxidation may take place (1) in powder (2) in solution.

When oxidation occurs in the dry ampoules, the powder loses its characteristic canary yellow colour and looks distinctly brownish as in picture B. In such cases cracks on the walls of the ampoules (often under the label) can always be found. If too small to be seen with the naked eye the suspected ampoule is to be immersed in alcohol. The alcohol will get in through the cracks. Such ampoules should always be discarded.

With oxidised solution also, the change of colour is noticeable, as shown in the picture B. Such solutions should be discarded at once.

Solu-Salvarsan

It is supplied in the form of a 10% ready-made

should be given up, or at least be sufficiently limited. He must be given a nourishing food. Physical and mental exertions are to be avoided during the course of the treatment, although regular exercise is very important.

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Besides, by proper selection of the site of injection, the painlessness can be still further ensured. In the adjoining picture (p. 16) the suitable sites are marked with crosses. Again, injection of the solution with a dry needle, *i.e.*, needle not moistened with Solu-Salvarsan is essential. Two needles, therefore, for every injection are to be kept ready one to aspirate the solution from the ampoule and the second dry one, only for giving the injection.

Some hesitate to inject Solu-Salvarsan intravenously This hesitation is due to the curious belief that Solu-Salvarsan owes its painlessness to the inclusion of some anaesthetic hence such solutions should not be given intravenously As has been explained above the painlessness of Solu-Salvarsan is due to a new process of manufacture, etc., and not due to any anaesthetic. Further it may be remembered that if Solu-Salvarsan actually contained an anaesthetic it would not be passed by the testing authorities referred to in this booklet elsewhere. (*See page* 21)

Dosage.

Salvarsan preparations are used in all forms of syphilis lesions of the primary secondary and tertiary stages, including the sequelæ of the same such as tabes and general paralysis. The earlier the full course of Salvarsan treatment is started the more favourable is the outlook for a real and permanent cure.

The following dosage is recommended per course

Adult —

Preparation.	Initial Dose.	Subsequent Dose.	Total quantity
Neosalvarsan			
Male	0.30 g.	0.45–0.60 g.	4½–6 g.
Female	0.15 g.	0.30–0.45 g.	4–5 g.
Solu-Salvarsan			
Male	3 cc.	4–5–6 cc.	50–60 cc.
Female	2 cc.	3–4 cc	40–50 cc.

Exact detailed scheme is to be found on *pages 25—26*

A total quantity of 4.5—6 grammes of Neosalvarsan or 40—60 cc. of Solu-Salvarsan is thus used, *i.e. on an average 10—15 injections. As a* rule, this is quite sufficient. Higher single dose than the above should not be given except in unusually healthy individuals. In any case owing to the constitutional differences in individual patients, it is not possible to adhere blindly to any standard scheme. In each case the physician has to adapt himself to the individual conditions of his patients and adjust the dosage accordingly. This individualization of the dosage will do away with most of the by-effects which were reported in the early Salvarsan days and which still ensue if the drug is not properly handled.

To complete a cure repeated courses are necessary with a 5—6 weeks' interval in between any two consecutive courses.

Child —

Age.	Preparation.	Initial dose.	Subsequent dose	Total dose.
2nd year	Neo.	0 05 g.	0 10—0 15 g.	1.5 g.
	Solu.	0.5 cc.	1 5 cc.	15 cc.
3rd year	Neo.	0 05 g.	0 10—0 15 g	2 g.
	Solu.	1 cc.	2 cc.	20 cc.
4th year	Neo.	0 10 g.	0 15—0.2 g.	2 5 g.
	Solu.	1 cc.	2 cc.	25 cc.
5th year	Neo.	0 10 g.	0 15—0.2 g.	3 g.
	Solu.	1.5 cc.	2 cc.	30 cc.

And so on, till by the 10th year the female adult dose is reached. For precise calculation of the dose by body weight see page 24.

Infant —*see schedule pages* 28, 29

Accessory Treatment.

Apart from the injection of Salvarsan ('Neosalvarsan or Solu-Salvarsan) preparations, modern treatment also calls to its aid other accessory drugs to quicken the course and to make it still more thorough. With this end in view bismuth, in its various forms, is usually resorted to.

Casbis an oily bismuth preparation manufactured in Hoechst, is to be particularly recommended for this purpose

The underlying principle of oily bismuth preparation like 'Casbis is that owing to its slow but

continuous absorption from the depôt formed by intramuscular injection, a steady influence is brought to bear on the spirochetes during the interval between two consecutive Salvarsan injections. For it must be remembered that although Salvarsan preparations act intensively they act for a short time only due to their quick excretion from the system. To remedy this gap in the continuous influence 'Casbis being an oily suspension, is pre-eminently suitable.

With 'Casbis the dosage also is very convenient. 1 cc. of the preparation contains 0·1 g. of bismuth and this dose is usually found to be sufficient. It is advisable to start the treatment with ½ cc. only and to carry on the course with 1 cc. subsequently per injection, until the content of one bottle containing 15 cc. is completely exhausted.

Before the introduction of bismuth treatment, mercury was used as an accessory to Salvarsan and it still has many adherents. The therapeutic principle is, more or less, the same.

Among the host of various mercury preparations on the market Salyrgan manufactured in Hoechst, has been found to be very convenient, effective and safe (see page 55) It can be given according to the same scheme as is done in case of 'Casbis or simultaneously with Neosalvarsan or Solu-Salvarsan with which it can be mixed in the syringe

In cases, however where treatment by injection, for one reason or other is not practicable peroral treatment may be resorted to by means of

Primary Care of the Prepuce.

Plate No. 6



Secondary 51 Lemon.

Spirocid also manufactured in Hoechst (*see page 54*)

Precautions in Arsenobenzol Treatment.

Before Salvarsan treatment is undertaken a thorough physical examination of the patient should be carried out as a routine measure. A painstaking examination of the heart and the urine (albumen, sugar, urobilinogen) must be specially carried out. Patient must be carefully questioned at the commencement of treatment as to previous illness and, if already treated with Salvarsan whether there was undesirable reaction* Throughout the course, especially on the days of injections, the patient should avoid all unaccustomed bodily strain as well as exercise of every description. It is advisable to allow the patient to rest on the couch for 15 minutes after the injection. During the course of treatment good nutrition must be maintained as far as possible.

Purgative in the previous night should be given and no solid food for 3—4 hours before the injection should be allowed. A small tumbler of glucose solution, half-an-hour before the injection, may be given with advantage. *For further particulars see Appendix.*

Testing of Salvarsan Preparations.

In spite of the close and careful attention on the part of the manufacturers to the details of G

* In case, idiosyncrasy is suspected according to the previous history (swellings on face or extremities after treatment, or skin eruptions during previous antisyphilitic treatment) the following test is to be carried out:—

⅛ cc. intracutaneous injection of 1 : 160,000 solution of Sola-Salvarsan or Neosalvarsan is to be given and reaction noted.

manufacturing proces of Neosalvarsan and Solu-Salvarsan' every batch of the finished products undergoes a fourfold test. These tests are carried out by the Institute for Experimental Therapy at Frankfort a/M/ an Institute controlled by the Government.

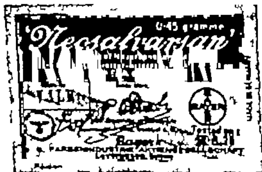
The tests are —

1. *Chemical* —Wherewith the purity of the product and the uniformity of its composition, particularly the standard arsenic content (viz. about 20 per cent.) are tested.
2. *Biological* —Wherewith determination is made on a series of animals about the toxicity and the curative effect of the batch tested for
   ( ) *Toxicity* determination is made by intravenous injection of the minimum lethal dose into mice and rats. The duration of observation is 3 days for mice and 6 days for rats. The findings are then arranged and compared with the standard value as obtained with the original Neosalvarsan
   (b) *Curative ffect* determination is made on mice artificially infected with trypanosomes and allied diseases and then treated with the particular sample tested for
   The batch of the preparation is considered sa-isfactory if the tested sample bows the same curative effect as that of original Neosalvarsan
3. *Cl ical*.—Wherewith the final test (made on actual syphilitic patients. For this purpose certain amount of different doses of the sample batch, already tested and found satisfactory are sent to public hospitals, controlled by the Stat If the clinical trials prove that the sample is as efficacious as the original 914 and that it is free

from all bye-effects, then and then only is the batch considered fit for the market and consequently released for general consumption.

It will be seen that all the Salvarsan products have to undergo manifold rigid tests and have to fulfil all the conditions pertaining thereto.

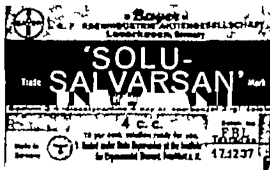
Note.—Every packing of Neosalvarsan and Solu-Salvarsan contains, on the label of the ampoule as well as on the outer carton-packing, batch number in letters, e.g., VUHV XXXV and so on (see picture below). The Neosalvarsan packing contains four such letters while Solu-Salvarsan packing, for the present, contains



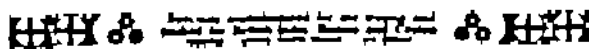
FACSIMILE OF LABEL.

only three. In case of any complaints from the users of a particular packing of Neosalvarsan or Solu-Salvarsan these letters give the manufacturers the clue to trace the relative batch and then to test specimen to find out if any explanation can be found for the complaints. Further on the bottom of every carton there are also numbers, e.g., 1768121, etc. Such numbers have no importance whatsoever in tracing the particular batch to which the suspected packing belongs; hence should not be referred to in case of correspondence with the agents or the manufacturers.

Date.—Every carton as well as the contained ampoule bears on the label particular date. (*See picture page 23.*) This is the date when the substance of the particular batch was tested by the Government authorities. Hence these dates *must not be confused with expiry dates as are found with serum packings.*



Finally the ampoules which are meant for sale in the tropics are prepared in a special way to stand the requirements of the climate. To safeguard against mistakes and also against illicit import of such packings which are not meant for import into the tropics, every packing of Neosalvarsan and Solu-Salvarsan sold for instance to India bears a special protective banderole facsimile of which is reproduced here



BANDEROLE.

Important.—Only the packings that contain the above special banderole are exchanged by the importers, Havero Trading Co. Ltd., in case of any genuine complaint with particular packing

III

Schedules of Treatment

(1) In Primary and Secondary Stages.

A. Standard Method.

First Course

	Men.	Women.
1st day	Neosalvarsan 0.3 g. ('Solu-Salvarsan' 3 cc.)	Neosalvarsan 0.15 g ('Solu-Salvarsan' [illegible] cc)
2nd day		
3rd day	Casbis ½ cc.	Casbis ½ cc.
4th day		
5th day	Casbis 1 cc	Casbis 1 cc.
6th day		
7th day	Neosalvarsan 0.45 g. ('Solu-Salvarsan' 4-5 cc)	Neosalvarsan [illegible] g. ('Solu-Salvarsan' 3 cc)
8th day		
9th day	Casbis [illegible] cc.	Casbis 1 cc.
10th day		
11th day	Casbis [illegible] cc	Casbis 1 cc.
12th day		
13th day	Neosalvarsan 0.45 g. ('Solu-Salvarsan' 4-5 cc)	Neosalvarsan [illegible] ('Solu-Salvarsan' 3 cc)

Proceed in this way until a total quantity of 4.5—6 g Neosalvarsan or 45—60 cc. of Solu-Salvarsan is administered.

After an interval of 4—6 weeks resume another course of treatment even if Wassermann reaction is negative.



NOTE:—In extensive skin eruptions of the secondary stage it is strongly advisable to give, during the first few days, only Casbis on alternate days and to begin with Salvarsan after the fourth Casbis injection. Thus Herxheimer reaction (see page 36) be voided.

Date.—Every carton as well as
bears on the label a particular date
This is the date when the subst
batch was tested by the Governme
these dates must not be confus
as are found with serum packings.



Finally the ampoules which are
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are not meant for import into the t
of Neosalvarsan and Solu-S
instance, to India bears a special
facsimile of which is reproduced be



BANDEROLE.

Important.—Only the packings th
special banderole are exchanged by t
Trading Co., Ltd., in case of any gr
a particular packing.

Plate No. 8



Ornament on the Forehead.

(7) In Tertiary and Latent Syphilis.

Patients in the tertiary or so-called latent stage are treated in practically the same manner as in cases of secondary syphilis. One exception is that they are not to be treated so intensively that is to say the intervals between the injections should be longer and the dose should be decreased. The course of treatment should be started with Osabis as the first injection. Secondly iodides ("Entodon or Sajodin") are to be used freely throughout. It often takes years to obtain a negative Wassermann reaction in these cases and the total medicament required is much greater than that in the secondary syphilis. Obviously therefore, treatment cannot be pushed with the idea of obtaining a negative result in a given time. Judgment must be displayed in arranging the dosage and the intervals between them.

(8) In Pregnancy

First Course.— Neosalvarsan every 5th day beginning with 0 15 g. followed up by 9 injections of 0 3 g.

or

Solu-Salvarsan beginning with 2 cc. followed by 8 injections of 3 cc.

Interval.—3—4 weeks.

Second Course.—Proceed in the same manner as in the first course. Osabis or Salyrgan may be given as usual in the intervals between any two consecutive or Solu-

Salvarsan Injections.

After Child Birth.—Treat the mother by any of the suggested schemes for primary and secondary syphilis. If the child has a positive Wassermann or other manifestations, resort to the schedule of treatment of congenital syphilis.

(4) *In Congenital Syphilis.*

Either Neosalvarsan or Solu-Salvarsan can be used for treatment in this connection although, considering the age of the patient and the scarcity of veins in such patients, Solu-Salvarsan only comes into practical consideration. To avoid too many injections the accessory treatment is best carried out with grey ointment instead of bismuth.

The dosage is determined according to the bodyweight of the child, 0 015 g of Neosalvarsan or 0 15 cc. Solu-Salvarsan per every 2 lbs. bodyweight. *The dose thus ascertained is given once weekly* The schedule of treatment given below is according to this dosage.

Grey Ointment.—It contains 33 per cent of metallic *mercury and is quite effective.*

Mode of Application.—One gram of grey ointment per 10 kg. of the bodyweight of the child is to be taken each day On the first day the chest and the upper extremities are to be rubbed, second day abdomen, third day upper portion of the back, fourth day lower portion of the back and fifth day the legs. On the sixth day cleansing bath is essential. This finishes the course of one application.

Generally 5 such courses of applications, as shown in the schedule, are required to complete the treatment.

Schedule of Treatment.

1st week	1st course of mercury treatment through grey ointment for 5 successive days.
2nd week	1st dose of Neosalvarsan or Solu-Salvarsan
3rd week	2nd dose of Neosalvarsan or Solu-Salvarsan
4th week	2nd course of grey ointment for 5 successive days.
5th week	3rd dose of Neosalvarsan or Solu-Salvarsan
6th week	4th dose of Neosalvarsan or Solu-Salvarsan
7th week	3rd course of grey ointment for 5 successive days.
8th week	5th dose of Neosalvarsan or Solu-Salvarsan
9th week	6th dose of Neosalvarsan or Solu-Salvarsan
10th week	4th course of grey ointment for 5 successive days.
11th week	7th dose of Neosalvarsan or Solu-Salvarsan
12th week	8th dose of Neosalvarsan or Solu-Salvarsan
13th week	5th course of grey ointment for 5 successive days.

This completes the treatment which is as thorough as can be expected.

In cases, however, where injection treatment is not practicable peroral treatment may be resorted to with Spirocid according to the scheme given in the following table. Spirocid being tasteless, can be dissolved in milk or sweetened tea.

For exact dosage *see schedule on pages 30-32.*

Salvarsan injections.

After Child Birth.—Treat the mother by any of the suggested schemes for primary and secondary syphilis. If the child has a positive Wassermann or other manifestations, resort to the schedule of treatment of congenital syphilis.

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Generally 5 such courses of pplications, as shown in the schedule, are required to complete the treatment.

Dose for bodyweight of

Days.	3.5 kg = 7 lbs.	5 kg = 11 lbs.	7 kg = 15.5 lbs.	9 kg = 20 lbs.
15	—	—	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
16	—	—	—	—
17	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)	—	—
18	—	—	—	—
19	—	—	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
20	—	—	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
21	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
22	—	—	—	—
23	—	—	—	—
24	—	—	—	—
25	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
26	—	—	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
27	—	—	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)
28	—	—	—	—
29	¼ tabl. (0.06 g.)	½ tabl. (0.125 g.)	—	—

Dose for bodyweight of

Days.	3.2 kg = 7 lbs.	5 kg = 11 lbs.	7 kg = 15.5 lbs.	9 kg = 20 lbs.
20	—	—	—	—
21	—	—	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)
22	—	—	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)
23	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)
24	—	—	—	—
25	—	—	—	—
26	—	—	—	—
27	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)
28	—	—	½ tabl. (0.06 g.)	½ tabl. (0.125 g.)
29	—	—	—	½ tabl. (0.125 g.)
Total amount	3½ tabl. (0.80 g. = gr. 12)	4 5/6 tabl. (1.20 g. = gr. 18)	6 7/12 tabl. (1.64 g. = gr. 24.75)	10½ tabl. (2.62 g. = gr. 39.25)

NOTE.—For children at the breast it is advisable to follow in the beginning the instructions for dosage given in Table I. If, however, no signs of intolerance to "Spirocid" have been observed, the larger doses in the first two columns of Table II may be administered without consideration of the fact that the doses in these columns are partly intended for heavier children. Owing to the great resistance of small children to arsenic, these relatively large doses are well borne without doing any harm and in many cases are to be recommended on account of their greater therapeutic effect.

If during treatment the child gains in weight, the previously calculated dosage should not be adhered to but should be increased according to the current bodyweight as per table.

II. Ready dosage table for the administrat. of "Sptrecid" tabl. of 0.25 g. (4 grs.) to children & adults.

Dosage according to bodyweight.

Days	10 kg = 22 lbs.	20 kg = 44 lbs.	30 kg = 66 lbs.	40 kg = 88 lbs.	Adults.
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible] total	[illegible] total	[illegible] total	[illegible] total	[illegible] total

(5) In Syphilis, complicated by Tuberculosis.

Syphilitic patients with pulmonary tuberculosis should not be debarred from Salvarsan treatment although the treatment should be done with great caution, for both the diseases exercise an unfavourable influence on each other

Prof. H. Schlesinger of Vienna recommends treatment by iodine for which purpose *Entodon* (manufactured in Elberfeld) or other iodine preparations can be used. Mercury or bismuth can be given along with iodine, but mercury should be confined to cases showing oedema as the result of cardiac decompensation. In such cases Salyrgan, with ammonium chloride is a valuable diuretic.

The author warns against the administration of arsenobenzols in large doses. He begins with 0 15 g Neosalvarsan or corresponding doses of Solu-Salvarsan twice a week, and increases this up to 0 3 g per dose. Treatment is stopped when a total of 3—5 g has been given. This course may be repeated after an interval of 8—10 weeks.

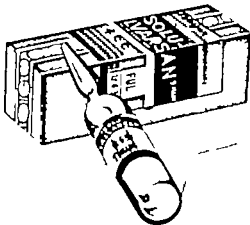
Prof. L. V Zumbusch, of Munich, on the other hand, while recommending small initial doses of 0 15 g Neosalvarsan at intervals of about 2 days, continues the course if these are tolerated until the normal total dosage of 6 g Neosalvarsan is reached.

Photo No. 9



Syphilitic Infant.

Plate No. 10



Schlesinger frequently obtained good results with the arsenical preparation Spirocid given by mouth in doses of one-half to three tablets per day (gr. 2 to gr. 12). After three days, a three days interval is interpolated and the treatment is continued according to this scheme until a total of 30 tablets of gr. 4 have been administered.

If the tuberculous foci are stationary and of long duration and the syphilis is recent, then the latter is treated as it would be in a patient with sound lungs. Very difficult of treatment is a recent syphilitic affection where the manifestations of tuberculosis are active. If the general condition of the patient is good, anti-syphilitic therapy should be commenced at once, but should the general condition deteriorate treatment must be discontinued. Later, a course of arsenic and bismuth or mercury may be undertaken. When the patient improves a course of 30 Spirocid tablets may be given.

IV

By Effects of Arsenobenzols

It is necessary for the physician to be well acquainted with all the possible by-effects that may manifest themselves during the course of arsenobenzol treatment.

So far as the by-effects, solely due to the drug itself, are concerned it should be noted that in recent years these have been practically eliminated. The long experience of the makers with the complicated details of the manufacturing process of Salvarsan compounds is now sufficient guarantee for safety. That is why the original preparations enjoy so much popularity everywhere.

There are however still a number of by-effects which are due to —

(1) Faulty technique

(2) Peculiarity of the patient or the disease.

(1) Faulty Technique.

(a) *Fever*—It may develop after the first injection of Salvarsan generally in the case of a recent infection. It begins about 8 to 10 hours after the injection with a typical rigor and lasts for about 4 hours. No special treatment except a few symptomatics is required.

This kind of fever is the result of reactions due to what are known as water faults *i.e.*, the impurities of the water with which the solution is prepared. It is obvious that sterile water contained in big bottles soon gets contaminated

through the access of air during repeated opening of the bottle as a result of this contamination what was originally sterile water, within a short time, swarms with various micro-organisms, usually of harmless type. The fever with its rigor is, therefore, to be compared to protein-shock. Dirty needles may also bring about the same train of symptoms hence strictest asepsis and greatest care with the instruments and materials are the best insurance against this sort of by-effect.

It may be mentioned, however, that there is a school of thought which looks upon the fever as a kind of Herxheimer reaction (see below).

(b) *Nitritoid Reactions.*—Symptoms known as nitritoid reactions, (so called because it was formerly believed that the amino group of Salvarsan was responsible for these reactions and although this view has now been discarded, the name remains) are of a more alarming nature although nowadays they are rarely met with. They manifest themselves shortly after the injection by flushing slight swelling of the face and the tongue, fullness in the head, coughing and nausea and may develop into dyspnoea, ultimately leading to unconsciousness, lasting for several minutes.

Urticaria on the head and the body with intense itching and burning is another symptom of this group of reactions.

These symptoms are signs of
tions and are due to improper

preparation of the patient or of the solution and its administration. Injections given too quickly or with too concentrated solution are mainly responsible for such reactions although, as far as urticarial rashes are concerned, in certain cases, these should be ascribed to the idiosyncrasy of the patient (*see below*).

Therapeutic measures against aforesaid by-effects.

(a) A subcutaneous injection of ½ cc. or 1 cc. of Suprarenin solution (1 1000) should be given at once. Suprarenin can also be used prophylactically in which case it should be injected before giving the Salvarsan injection.

(b) Rest in bed, discontinuance of further injections until the fever subsides (2—3 days) and administration of a mild antipyretic like Pyramidon or Novalgin

(2) Peculiarity of the Patient or the Disease.

(a) *Herxheimer's Reaction.*—It is mostly seen at the early secondary period and is characteristically seen shortly after the injections when the eruptions assume a definitely acute appearance. An ordinary roseola, for instance, changes its turbid brownish colour into an inflamed red and a temporary clinical exacerbation, usually of a local character is met with. This reaction signifies rapid destruction of the micro-organisms, resulting in a protein shock ("local reaction"). It may occur with any anti-syphilitic drug. *Specific treatment with*

drugs therefore, need not be interrupted but only the individual dosage should be slightly reduced, and the interval between injections prolonged. Sometimes it is necessary to use, for a few weeks, less intense remedies like Casbis

(b) *Neuro-Recidives.*—If an anti-syphilitic treatment is resumed after an interval of a long period, during which the symptoms were latent, a sudden reaction of the nervous system, as a result of the renewal of the treatment, may occur. These may assume the character of peripheral neuritis or of central symptoms. This proves that the nervous system of the patient, or at least a part of it, has been, in the meantime, attacked by the spirochaetes although the symptoms were not yet manifest. However this flaring up of the symptoms through treatment demands continuation of the anti-syphilitic measures and not the suspension of the same, although, for the time being, intensive treatment or strong preparations like Salvarsan may be replaced by a milder preparation like Casbis

(c) *Dermatitis.*—The most important complication in this group is the so-called late dermatitis, which develops 8 to 10 days after the 2nd or 3rd injection. The first symptom, which always announces the impending complication, is severe itching all over the body. Fever develops next and precedes the rashes for a few days. *As soon as itching appears* Salvarsan has to be suspended immediately and treatment with Casbis started.

The first *local* symptom of the dermatitis is red maculous exanthema on the flexor

limbs and on the body. The eruptions develop into papules which very soon become moist oozing out a sticky secretion which on drying forms yellow scales. The face is generally swollen, itching is intense, movement of the body painful. After 10—14 days, under proper treatment, the condition improves and the skin gradually heals up.

In some cases, however, a more serious development takes place. Fever persists and goes higher even reaching 103°—104° F., indicating that a secondary infection has taken place. Still larger parts of the skin develop a true moist dermatitis with, more or less, intensive desquamation of the upper layers of the skin. There is general prostration, hair begins to fall off and the nails on the fingers and toes become severely disfigured. In some cases the mucous membranes of the mouth, nose and pharynx are inflamed and the process may extend into the upper airways, quickening a fatal termination. The secondary staphylococcal infection which is directly responsible for this kind of dermatitis may in a certain percentage of cases, develop into a general sepsis and the patient dies.

Cause.—A natural or acquired idiosyncrasy of the patient is responsible for this condition. The latter may develop if the injections are given with a wet needle, for in its passage through the tissues during injection, the needle carries a trail of arsenic solution which sensitizes the skin and the sub-skin structures. (See suggestion on *page 17*.)

Treatment.—The main point is to prevent the development of the secondary infection. All

arsenical treatment has to be stopped as soon as the patient complains of itching, even if there be no skin symptoms. If, however, the skin eruptions have already appeared the patient should be confined to bed and treated with sodium thiosulphate which has proved effective in such cases. It can be administered orally as well as by intravenous injections. Orally 3 grams thrice daily is to be taken. For intravenous injection give 0 75—1 0 gram in 10 cc. of distilled sterile water once daily

A warm bath containing potassium permanganate proves to have a soothing effect on the skin. After the bath the skin should be dried and powdered with talc. The patient should be given copious drinks. Perspiration may also help to ameliorate the trouble.

Latest researches show that in arsenodermatitis, a functional disturbance of the liver is often involved. Treatment with liver extract ("Campolon"*) is, therefore, fully indicated, and has already given excellent results indeed. The treatment is to give 1 injection of 2 cc. (1 ampoule) daily for a few weeks, then on alternate days for a week, then about every fourth day With this method the dermatitis subsides very soon whereafter in many cases, the Salvarsan treatment can be resumed.

In combating the general symptoms it is essential to take great care of the heart of the patient.

*CAMPOLON :—Highly potent, well-tolerated liver extract, suitable for injection. Quick increase in the number of erythrocytes, quick improvement in the general condition, even where oral liver therapy has been unsuccessful, takes place.

Daily normal saline infusions help to lessen the toxic effects. Calcium preparations intramuscularly or intravenously have proved very beneficial. Proper nursing and diets are also important factors.

In milder forms of eruptions no special treatment is necessary. Only suspension of Salvarsan and complete rest will do. If required Suprarenin and warm baths may also be tried.

(d) *Jaundice.*—Sometimes, jaundice appears during the course of arsenobenzol treatment. If after the first injection, it is simply due to Herxheimer's reaction. This type of jaundice, however disappears when antisyphilitic treatment is continued. But jaundice occurring during the later stage of arsenobenzol treatment may be of a graver type. In this case one must stop all specific treatment because continuation with the same is apt to produce yellow atrophy of the liver.

Treatment.—First stop arsenobenzol treatment entirely, give saline laxative and treat the patient for catarrhal jaundice. If it does not clear up in a short time carry on the anti-syphilitic treatment by means of Hg ('Salyrgan') or Bi ('Casbis'). In case the jaundice is due to a syphilitic disease of the liver this treatment will shortly clear up the symptoms and afterwards Salvarsan treatment may be resumed.

Sometimes jaundice occurs 2—3 weeks after the completion of the course of Salvarsan treatment. In this case it may be due to relapse of the disease or due to Salvarsan intoxication. To decide the cause, Wassermann reaction or Kahn test may be resorted to.

V

Further Indications for Salvarsan Products.

Apart from syphilis, Neosalvarsan and Solu-Salvarsan have proved of value in many other diseases which are usually rampant in tropical countries. The following are some of the main indications —

1 Yaws.

(*Ceylon* Parangi *Medical Name* Framboesia.)

Yaws is a chronic infectious disease caused by the *spirochaeta pertenue*, which closely resembles the syphilis *spirochaeta*. In India, yaws is epidemic in all the jungle areas particularly Orissa, Central Provinces, the extreme South, Assam and Ceylon. Just like syphilis, yaws has also three distinct stages —

Primary secondary and tertiary

To a certain extent it may be considered as a sister disease to syphilis, although it is definitely not a venereal disease.

The primary sore may appear anywhere on the body usually at the site of some old skin lesion, mostly extragenital, in the form of a papule 1—7 cm. in diameter. It becomes covered with yellowish secretion or a crust. The early secondary stage is characterised by skin eruptions of polymorphic nature. Papules of granular form appear on the skin. In most cases the disease

develops affecting the superficial tissue and producing big ulcers of the skin. These develop further to affect the muscles and periosteum. The papules on the soles and palms are specially characteristic resulting in deep fissures of the horny layers. In the tertiary stage of yaws the bone tissue may be deeply affected and greatly damaged. There is no congenital type of yaws.

Treatment —The treatment of choice is Neosalvarsan or Solu-Salvarsan. Formerly it was believed that a few injections cured the disease. However latest researches have shown that prolonged treatment like that in syphilis is indispensable to effect a genuine cure. The same schedule of treatment is to be followed although Casbis may be omitted. Certain obstinate cases of tertiary stage may require repeated courses to achieve the desired effect. Still the disease responds quickly to treatment and there are many countries where yaws has been practically stamped out.

For peroral treatment, Spirocid may be resorted to *See page* (54).

2. Relapsing Fever

It is an acute infectious disease which begins suddenly with rigor and fever and subsides with crisis and profuse sweating after 1—7 days but recurs at intervals of from 3—7 days for a very long time. It is caused by the *Spirillum Obermeier* found in the blood. It is transmitted by lice or bed bugs. In India epidemics occurred in the Central Provinces and the North Western Frontier.

Plate No. 11

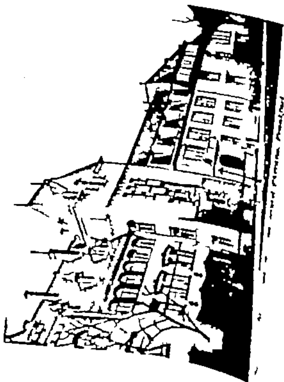


Plate No. 12



Treatment.— Neosalvarsan and Solu-Salvarsan have proved to be specific against it. Generally one injection cures the disease. In rare cases two or more injections are required. Injection has to be given when *the temperature is rising.* To give Salvarsan when the crisis approaches is dangerous on account of violent reaction. If the first opportunity is missed one should wait until the next relapse when the injection during the rigor is to be given.

Recently Spirocid tablets (4 grs.) in doses of 4—6 daily were found to be very efficacious. In cases of collapse Suprarenin injection (0.5 to 1 cc. of 1 1000 solution) may be given subcutaneously

2. Rat Bite Fever

It is a chronic relapsing type of fever. The causal agent is named *spirillum Morsus Muris* transmitted to man by the bite of infected rat.

Symptoms.—After the bite, the wound disappears uneventfully However within 2 to 4 weeks, the site of the bite starts paining again and the scar breaks up once more. The regional lymph glands swell up. A definite ulcer is developed along which small vesicles appear. The temperature rises to 103°F with rigor, nausea headache, pain in the joints and diarrhoea. The fever remains so for 8 days and then the temperature drops and the symptoms ameliorate. Relapses appear at varying periods.

Treatment.— Neosalvarsan or Solu-Salvarsan should be administered. One or

injections are usually sufficient to bring about a permanent cure.

4. Malaria.

The nature of the disease is too well-known to call for description. Neosalvarsan and Solu Salvarsan are particularly useful in neglected chronic cases which do not rapidly respond to quinine here Salvarsan besides its definite tonic action, seems to activate the tissue and to re-establish the efficacy of quinine. 2—3 injections only are required.*

5. Coccal Infection of the Urinary Tract.

Latest researches have revealed that Salvarsan preparations have an excellent effect in the coccal infections of the urinary tract. In case where the virulence of the parasites depends upon the alkaline reaction of the urine Salvarsan preparations prove almost specific. The action of these preparations ('Neosalvarsan and Solu-Salvarsan') is specially striking in infections with cocci such as staphylococcus albus, streptococcus and pneumococcus.

6. Vincent's Angina.

It is a disease of sub-acute character causing an ulcerative tonsillitis with regional oedema on the pharynx. The ulceration closely resembles syphilitic affections of the second stage, but diagnosis depends on the more inflamed character of the

* Atebrin—a potent synthetic drug, is now recognised to be the best for all types of Malaria.

affection. The disease is caused by a *spirochaeta refringens* and a peculiar form of *bacillus fusiformis*. The two organisms live in close symbiosis.

This very painful and distressing disease heals after 1 2 injections of Neosalvarsan Local application of the drug (Neosalvarsan in 10 per cent solution) has some merits but is not so efficient as the injection.

7 Phagedaenic Ulcers.

(*Tropical Ulcer Field Sore*).

These ulcers are usually situated in the lower portions of the leg These are caused by the same parasites as Vincent s Angina defying all kinds of treatment. Energetic Salvarsan treatment combined with local treatment (surgical excision, Rivanol & Padutin) brings about the desired effect.

8. Gonorrhœa.

French authors successfully employed Salvarsan in *small* doses in gonorrhoeal complications (epididymitis, prostatitis, etc.) Solu-Salvarsan can be recommended for this indication.

APPENDIX I.

Directions for the use of Salvarsan Preparations

(In connection with the regulations made by the German Health Council.)

I. The main conditions for successful use of Salvarsan preparations are complete mastery of the necessary technique.

Before treatment, a thorough investigation must be made as regards the heart, the urine, previous diseases etc. If acute disturbances of health of a serious nature are present, Salvarsan injections must be withheld completely. Especial care is necessary in patients showing symptoms of severe anaemia and extreme under nourishment, in status thymolymphaticus, diabetes, goitre exophthalmic goitre Addison's disease pulmonary tuberculosis, cardiac, circulatory renal and hepatic disorders (in case of doubt, functional test of these organs should be performed), digestive disturbances, adiposity alcoholism, epilepsy and during pregnancy In these cases test doses should at first be used if good tolerance is shown then only the usual dosage is to be adopted.

II. The size of the individual dose is determined by the body-weight, the general state of health and the severity and extent of the disease

III. Salvarsan injections should not be given on an empty stomach nor on full stomach. During treatment, particularly on the days injections are given, patients should avoid unaccustomed physical exertion and excesses They should be told to pay

attention to disorders such as headache, general indisposition, dizziness, vomiting, fever fainting fits, flushing haemorrhages, skin rashes and decrease in the quantity of urine passed and if any of these occur to report to the physician immediately

IV If any of the disorders mentioned in paragraph 3 appear (and are not attributable to other reasons) treatment should be interrupted to be resumed only with small doses at least 8 days after the usual state of health has been regained. A transient rise in temperature (even rigor) after the first injection does not necessitate interruption of the drug, but increased temperature during the further course of treatment requires careful observation. Appearance of the so-called vasomotor symptom-complex during or immediately after an injection during the course of the treatment must be carefully considered (smaller doses, change of the preparation, subcutaneous injection of 1 mg Suprarenin 10 minutes before the next injection)

If exanthemata develop treatment must be interrupted immediately for at least 14 days. Slight rashes often subside after intravenous injection of 6-10 cc. of 10 per cent. sodium thiosulphate solution. In case of general dermatitis, stop the injections completely and consult a specialist before resuming treatment (great care necessary). When mercury and bismuth are given concurrently th by-effects of these preparations must be watched.

V The solution of Neosalvarsan must be prepared immediately before the injection is made. The solution must be absolutely clear and is preferably injected with an all-glass syringe. All Salvarsan preparations decompose and increase in toxicity in contact with air the solution must therefore b

injected immediately The contents of faulty ampoules, the remains of previously opened ampoules and discoloured preparation must not be used.

VI All traces of the solution must be wiped off the surface of the needle before an injection is given. The injection should be made slowly in debilitated patients or where heart trouble is present the injection should take several minutes. At the least complaint of pain or sign of infiltration (weal formation), or on the slightest manifestation of respiratory trouble rush of blood etc., the injection should be immediately stopped. If an obstruction is noticed when emptying the syringe, interrupt the injection immediately and before resuming the injection, make certain, by aspirating blood into the syringe, that the needle is in the right position in the vein and not paravenous.

Dalnow successfully used Cantan in one case of arsenobenzol intolerance and 3 cases of arsenical dermatitis. Cantan was given in a mixed syringe with Neosalvarsan Dreyfus on the basis of his extensive xperiments, recommends the injection of 'Tonophosphan solution in cases of arsenobenzol intolerance. Intramuscular injections of Campolon during the suspension period has also been used to combat intolerance to arsenobenzol treatment. Thus Rajam points out its remarkable utility in all cases of arsenical dermatitis. Indeed as he says the administration of 'Campolon is now a routine method of treatment in his clinic for patients suffering from dermatitis.

APPENDIX II.

CASBIS

(REGD. TRADEMARK.)

Description.— Casbis is a specially prepared activated hydrate of bismuth. It is sold in a sterile, oily suspension, ready for use. In the improved form, the substance remains evenly suspended in the oil. This makes for accurate dosage and uniform action.

Indication.—Primary and secondary syphilis.

Dosage and Administration.— Casbis is given by the intramuscular route. First 0.5 cc. is injected, then 1 cc. The total dose for a course amounts to 12—15 cc. which can, however be increased without harm up to 20 cc. in adults. Children get according to their age and general condition, first 0.05 cc., then 0.1 cc.—0.2 cc. and a total dose of about 1.5 cc.—2 cc. for a complete course. 1—3 days interval is generally given between the injections.

The bottle should be *well shaken before* use.

Original Packings —Bottles of 15 and 100 cc.

ENTODON'

(Regd. Trademark.)

Description.—'Entodon is a clear watery solution and contains 0.118 g (gr 1⅞) iodine in 1 cc. As the iodine in Entodon is combined with nitrogen, good tolerability is guaranteed by the uniform liberation of iodine in the system.

Indication.—Mainly secondary and tertiary syphilis, specially in neuralgic pains of tabes, headaches of cerebral syphilis, feeling of oppression in syphilitic aortic diseases.

Also in syphilitic articular disease, Entodon causes an alleviation of the complaint.

Further indications are —Bronchial asthma, emphysema, chronic bronchitis, hemiplegia, atheroma, hypertonia, septic pneumonia.

Dosage and Administration.—It can be given subcutaneously intramuscularly and intravenously One ampoule of 2 cc. daily or every 2nd or 3rd day

Original Packing.—Box of 10 ampoules of 2 cc. each.

SAJODIN

(Regd. Trademark.)

Description.—It is a stable and tasteless [illegible] preparation for peroral use in place of potassium iodide. It is well tolerated even by the most delicate stomach.

Indication.—Same as those of Estodin.

N.B.— Sajodin is to be specially preferred to other preparations where a sudden reaction would be attended with danger, e.g. in laryngeal affections, in cerebral syphilis, and in psychoses with a syphilitic basis.

Dosage and Administration.—1—2 tablets or ½—1 g. twice or thrice daily one hour after meals. The daily dose may if necessary be increased to 4—5 g.

Original Package.—Tube of 20 tablets of 0.5 g. (gr. 7½).
Bottle of 1 oz. powder.

'SPIROCID'

(Regd. Trademark.)

Description.— *Spirocid* is a white tasteless powder insoluble in water and is therapeutically allied to Salvarsan. It is stable in air and is easily absorbed by the digestive tract when given perorally. Spirocid is thus a peroral antisyphilitic to be used whenever Salvarsan preparations cannot be resorted to.

Indication.—1. Syphilis in its manifold complications particularly of congenital type.

2. Framboesia (yaws), relapsing fever, Vincent's angina, mumps.
3. Amoebic dysentery, leucorrhoea.
4. Anemia and other exhausting conditions following infectious diseases.

Dosage and Administration.—*Adults* —3—4 tablets generally per day.

Infants and children —½—2 tablets according to the bodyweight of the patient. For every 2¼ lbs. of bodyweight 0.25 g *i.e.* one tablet is to be used during the course of treatment. Thus for a child of 22 lbs., the total quantity to be consumed during the course is 10 tablets =2.5 g.

The daily dose is to be administered all at once early in the morning on empty stomach. In infants and small children, the daily dose may be given in the form of disintegrated tablet suspended in milk or sweetened water.

Original Packing.—Bottle of 30 tablets of 0.25 g (gr. 4) each.

SALYRGAN

(Regd. Trademark.)

Description.—Chemically it is a complex compound of mercury It does not produce any pain even after frequent successive injections nor is there any infiltration at the site of injection, as is usual with most of the current soluble salts of mercury

Indication.—Secondary and tertiary syphilis, in all forms of cardiac dropsy renal dropsy ascites, polyserositis, etc.

Dosage and Administration.—It can be given intravenously as well as intramuscularly

For an energetic therapy however, intravenous route should be preferred. The intramuscular injections are best made into the gluteus maximus. Precautions should be observed not to damage any nerve. (*See Picture on page* 16.)

For intramuscular as well as for intravenous injection the same doses can be employed. For adults between 0.5 to 2 cc. of the solution (10 per cent) as supplied in ampoules children receive proportionately less. In pure mercurial treatment (syphilo-therapy) it is suitable t..

with 0.5 to 1 cc. of Salyrgan and then inject at intervals of two days, i.e., thrice weekly a total of 5—9 doses of 1—2 cc. of Salyrgan

Original Packings—

Box of 5 amp of 1 cc.
Box of 10 amp of 1 cc.
Box of 5 amp. of 2 cc.
Box of 10 amp. of 2 cc.

NOTE :—As Salyrgan does not decompose when mixed with solution of Salvarsan preparations, it can be administered as mixed injection with any Salvarsan preparation. For mixed injection, the required preparation of Salvarsan is dissolved first in 3—4 cc. of water and drawn into the syringe, then from the freshly passed ampoule of Salyrgan 1—2 cc. are drawn up through the same needle and the two solutions are mixed up in the syringe by shaking. The mixture should be clear or t the most, opalescent.

THE SCHEDULE OF THE PREPARATIONS MENTIONED IN THIS BROCHURE TOGETHER WITH CURRENT PRICES

NEOSALVARSAN

Simple Ampoules	Per amp. Rs. a. p.	Per doz. Rs. a.
Amp. of 0 15 gm Dose I (94201)	1 1 6	13 4
Amp. of 0.3 „ Dose II (94202)	1 7 8	17 12
Amp. of 0 45 „ Dose III (94203)	1 10 4	19 12
Amp. of 0 6 „ Dose IV (94204)	2 0 4	24 4
Amp. of 0 75 „ Dose V (94205)	2 4 8	27 8
Amp. of 0 9 „ Dose VI (94206)	2 10 8	32 0

Clinical Packings	Per box Rs. a.
Boxes of 10 amp. of 0 15 gm Dose I (94201)	10 6
Boxes of 10 „ 0.3 „ II (94202)	14 4
Boxes of 10 „ 0 45 „ III (94203)	16 12
Boxes of 10 „ 0 6 IV (94204)	19 4
Boxes of 10 0 75 „ V (94205)	21 12
Boxes of 10 „ 0 9 „ VI (94206)	25 8
Boxes of 50 amp. of 0 15 gm Dose I (94201)	49 12
Boxes of 50 0.3 „ II (94202)	66 12
Boxes of 50 „ 0 45 „ III (94203)	74 4
Boxes of 50 0 6 IV (94204)	81 8
Boxes of 50 0 75 V (94205)	103 8
Boxes of 50 0 9 VI (94206)	120 8

Iso-Double Ampoules		
Amp. of 0 15 gm Dose I	(94211)	1 8
Amp. of 0 3 gm Dose II	(94212)	1 12
Amp. of 0 45 gm Dose III	(94213)	2 4
Amp. of 0 6 gm Dose IV	(94214)	2 12

SOLU-SALVARSAN—

(Ready-made 10% solution for intramuscular and intravenous injection, same content as in Neosalvarsan.)

Single Ampoules		Per amp.			Per doz.	
		Rs.	a.	p.	Rs.	a.
Amp. of 0 5 cc.	(24810)	0	12	6	10	6
Amp. 1 cc	(24801)	0	13	6	10	0
Amp. 2 cc	(24802)	1	2	0	12	8
Amp. 3 cc	(24803)	1	12	6	21	0
Amp. 4 cc	(24804)	2	1	6	25	0
Amp. 5 cc	(24805)	2	7	0	30	0
Amp. 6 cc	(24806)	2	11	0	33	0

Clinical Packings		Per box	
		Rs.	a.
Boxes of 10 amp. of 1 cc	(24801)	8	0
Boxes of 10 amp. of 2 cc	(24802)	11	0
Boxes of 10 amp. of 3 cc	(24803)	17	0
Boxes of 10 amp. of 4 cc	(24804)	20	0
Boxes of 10 amp. of 5 cc	(24805)	23	0
Boxes of 10 amp. of 6 cc	(24806)	28	0

CASBIS— (10070)

(Only Bismuth preparation for Syphilis treatment)

	Per	Rs.	a.
Bottles of 15 cc	bot.	3	8
Bottles of 100 cc	bot.	20	2

SALYRGAN— (15000)

(Well tolerated and highly renowned mercury diuretic)

		Rs	
Boxes of 5 amp. of 1 cc	box	3	10
Boxes of 10 amp. of 1 cc	box	6	7
Boxes of 5 amp. of cc	box	3	12
Boxes of 10 amp. of 2 cc	box	6	10

SPIROCID— (15183)

(Peroral arsenic preparation for syphilis, framboesia, sarcina, amoebic dysentery)

Bottles of 20 tabl. of 0.25 g (gr 4)	bot.	2	1

ENTODON— (11624)

(The ideal iodine preparation for parenteral use)

		Rs.	a.
Boxes of 10 amp. of 2 cc	box	8	0

RAJODIN—

(Iodine preparation, suitable for extended peroral iodine-treatment)

		Per	Rs. a.
Bottles of 1 oz.	(13904)	bot.	5 13

TABLETS—

Tubes of 20 tablets of 7½ gr.	(13905)	tube	3 0

CAMPOLON AMPOULES— (10409)

(Injectable liver-extract, 2 cc = 1 lb. fresh liver)

	Per	Rs. a.
Boxes of 5 amp. of 2 cc	box	4 11
Boxes of 25 amp. of 2 cc	box	22 14
Boxes of 100 amp. of 2 cc	box	81 0
Boxes of 3 amp. of 5 cc	box	5 14
Boxes of 15 amp. of 5 cc	box	28 0
Boxes of 50 amp. of 5 cc	box	80 0

SUPRARENIN HYDR. SOLUTION 1 1000

(The reliable Adrenalin brand) (13900)

(ORGANIC OR SYNTHETIC AS REQUIRED)

	Per	Rs. a.
Bottles of ½ oz.	bot.	1 11
Bottles of 1 oz.	bot.	2 4
Boxes of 10 amp. of 1 cc	box	2 12

Any alterations in the prices listed above shall be duly intimated.

AMBOCEPTORS FOR THE WASSERMANN REACTION

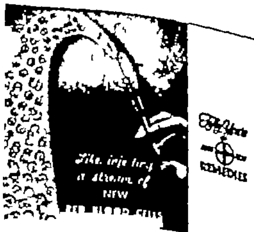
	Per	Rs. a.
TITRE OF 1 1000 TO 1 2000 (81903)		
Bottles of 1 cc	bot.	2 0
Bottles of 5 cc	bot.	6 10
TITRE OF 1 2000 TO 1 4000		
Bottles of 1 cc	bot.	6 1
Bottles of 5 cc	bot.	27 4
TITRE OF 1 4000 TO 1 6000		
Bottles of 1 cc	bot.	10 2
Bottles of 5 cc	bot.	46 8

2. EXTRACTS FOR THE PRECIPITATION TEST ACCORDING TO KAHN (83778)

ALCOHOLIC EXTRACT OF OX HEART WITH CHOLESTERIN

	Per	Rs. a.
Bottles of 10 cc	bot.	4 [illegible]
Bottles of 50 cc	bot.	17 [illegible]




Like injecting
a stream of
NEW